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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/518,128	08/29/2005	Bronislava Gedulin	0402US-UTL	7370

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Intellectual Property Department
Amylin Pharmaceuticals, Inc.
9360 Towne Centre Drive
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EXAMINER	
LI, RUIXIANG	
ART UNIT	PAPER NUMBER
1646	
MAIL DATE	DELIVERY MODE
12/30/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/518,128	GEDULIN ET AL.	
	Examiner	Art Unit	
	RUIXIANG LI	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 December 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5-12,14-30 and 32* is/are pending in the application.

4a) Of the above claim(s) *7 and 15-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5,6,8-12,14,22-30 and 32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/02/2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/02/2009 has been entered. Claims 1-3, 5-12, 14-30, and 32 are pending. Claims 1-3, 5, 6, 8-12, 14, 22-30, and 32 are under consideration. Claims 7 and 15-21 are withdrawn from consideration.

Withdrawn Objections and/or Rejections

The rejection of claims 1-3, 5, 6, 8-12, 30, and 32 are rejected under 35 U.S.C. 112, first paragraph for new matter is withdrawn in view of amended claims.

Information Disclosure Statement

The information disclosure statement filed on 12/02/2009 has been considered by the Examiner and a signed copy of the form PTO-1449 is attached to the office action.

Continuing Data

The filing data of PCT/US03/18657 provided by Applicants in is not consistent with PTO records. The FORM PTO-1390 filed by Applicants on 12/14/2004 indicates that the international filing date of PCT/US03/18657 is April 24, 2003, whereas the PTO records indicate that the international filing date of PCT/US03/18657 is 06/13/2003. Moreover, the oath/Declaration filed on 08/29/2005 indicates that 10/518,128 was filed on December 14, 2004, whereas the PTO records indicate that the filing or 371(c) date of 10/518,128 is 08/29/2005.

It's noted that Applicants have not addressed the issue, which is noted in the previous office action.

Claim Rejections Under 35 U.S.C.§112, 1st Paragraph

(i). The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

(ii). Claims 22 and 24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

Claim 22 recites a limitation, "wherein said active fragment comprises amino acids 22-36 of the amino acid sequence set out in SEQ ID NO: 2", whereas claim 24 recites "wherein said active fragment comprises amino acids 13-36 of the amino acid sequence set out in SEQ ID NO: 2". The two limitations introduce new matter. There is no support for such a limitation in the application as filed.

(iii). Claims 1-3, 5, 6, 8-12, 30, and 32 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. This rejection is restored due to the removal of the limitation in claim 1, "wherein said active fragment comprises amino acids 22-26 of the amino acid sequence set out in SEQ ID NO: 2" (the limitation introduces new matter).

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof.

Claims 1-3, 5, 6, 8-12, 30, and 32 are drawn to a method of treating, ameliorating, preventing, or protecting from an intestinal damage, said intestinal damage comprising an ulceration, said method comprising administering peripherally a pharmaceutically active formulation of PYY or a PYY agonist to a human, wherein said PYY or said PYY agonist is a peptide that comprises an active fragment of PYY. The specification defines PYY as a peptide YY polypeptide obtained or derived from any species, and defines PYY agonist as any compound which elicits an effect of PYY to protect from or reduce colon injury associated with inflammatory bowel disease or ulcerative colities and which binds specifically in a Y receptor assay or in a competitive binding assay (page 10). Thus, the claims are drawn to a method comprising administration of PYY or a genus of structurally undefined PYY agonists because the limitation "wherein said PYY or said PYY agonist is a peptide that comprises an active fragment of PYY" recited in the claims says nothing about the characteristic structure of the PYY agonists.

The specification fails to provide any critical structural feature to adequately describe the genus of PYY agonists that may be administered in the claimed method. The specification merely discloses two compounds, a human PYY of SEQ ID NO: 2 and PYY (3-36) of SEQ ID NO: 3, which are not sufficiently representative of the genus of PYY agonists. There is no disclosure of a defined relation between function and structure of the PYY agonists. There is even no identification of any particular portion of the structure that must be conserved. While the claims require that PYY agonist comprise an active fragment of PYY, it does not say what the active fragment is.

Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the genus of PYY agonists.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). As discussed above, the skilled artisan cannot envision the detailed chemical structure of the encompassed genus of the PYY agonists, and therefore conception is not achieved until reduction to practice has occurred. Therefore, only the method of administering PYY and PYY (3-36), but not the full breadth of the claims meets the written description provision of 35 U.S.C. §112, first paragraph.

(iv). Claims 1-3, 5, 6, 8-12, 14, 22-30, and 32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating, ameliorating, or protecting from an intestinal damage, comprising peripherally administering a pharmaceutically active formulation of PYY or PYY(3-36) to a human to treat or alleviate the intestinal damage, does not reasonably provide enablement for the claimed invention commensurate in scope with the claims (see below). The specification

does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and or use the invention commensurate in scope with the claims.

The factors considered when determining whether a disclosure satisfies enablement requirement include: (i) the quantity of experimentation necessary; (ii) the amount of direction or guidance presented; (iii) the existence of working examples; (iv) the nature of the invention; (v) the state of the prior art; (vi) the relative skill of those in the art; (vii) the predictability or unpredictability of the art; and (viii) the breadth of the claims. *Ex Parte Forman*, 230 USPQ 546 (Bd Pat. App. & Int. 1986); *In re Wands*, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

Claim 1 is drawn to a method of treating, ameliorating, preventing, or protecting from an intestinal damage, comprising administering a pharmaceutically active formulation of PYY or a PYY agonist to a human to treat, alleviate, or preventing the intestinal damage, wherein said PYY or said PYY agonist is a peptide that comprises an active fragment of PYY. Claims 2, 3, 5, 6, 8-12, 14, 22-30, and 32 depend from claim 1. The claims are broad because they are drawn to a method comprising administration of PYY or a genus of PYY agonists, without a specific structural limitation for the PYY agonists. The claims not only encompass a method of treating an intestinal damage, but also preventing an intestinal damage.

The specification discloses that reduction of colon injury of animal model for inflammatory bowel disease by peripheral administration of PYY(3-36) (Example 1; page 7, the 3rd paragraph). However, the specification does not provide guidance and working examples with respect to *preventing* an intestinal damage by administering PYY or a PYY agonist. Moreover, the specification fails to provide sufficient guidance and working examples on how to make and use the genus of PYY agonists. The specification does not disclose the amino acid residues which are critical for the PYY agonist activity defined in the instant specification. While the prior art teaches PYY agonists (e.g., US patent No. 5,912,227, 5,916,869, 6,017,879, WO 03/026591), they are not taught in the same context of protecting from or reducing colon injury associated with inflammatory bowel disease or ulcerative colities and binding specifically in a Y receptor assay or in a competitive binding assay..

The prior art teaches treating gastrointestinal disorders that are associated with excess intestinal electrolyte and water secretion as well as decreased absorption, such as infectious or inflammatory diarrhea, or diarrhea resulting from surgery comprising administering to a human a pharmaceutical formulation comprising PYY (Balasubramaniam, US Patent No. 5,604,203, Feb. 18, 1997). The prior art also teaches that peripheral administration of PYY or PYY(3-36) inhibits pancreatic exocrine and gastric acid output in mongrel dogs (Yoshinaga et al., *Am. J. Physiol.* 263:`G695-701, 1992), reduces body weight in 12-week-old mice (Morley et al., *Life Sci.* 41:2157-2165, 1987).

In view of the complexity of the nature of PYY-related compounds, it is unpredictable whether a compound that is related to PYY would work in the same manner as that of PYY. Therefore, it would require undue experimentation for one skilled in the art to make and use the invention commensurate in scope with the claims.

Response to Applicants' argument

Applicants argue that in Example 1 discloses that in pre-treatment of animals with PYY[3-36], prior to administration of agents that otherwise induce ulceration, results in prevention of the ulceration.

Applicants' argument has been fully considered, but is not deemed to be persuasive because working example 1 (Figs. 1-2; paragraphs [0061], [0062]) shows the reduction of colon injury of animal model for inflammatory bowel disease using PYY[3-36]; it does not show that PYY or PYY agonists may be used to prevent an intestinal damage associated with a condition, such as inflammatory bowel disease.

Claim Rejections Under 35 U.S.C.§102 (b)

(i). The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(ii). Claims 1, 2, 5, 10-12, 22-30, and 32 are rejected under 35 U.S.C. 102(b) as being anticipated by Balasubramaniam (U. S. Patent No. 5,604,203, Feb. 18, 1997)as evidenced by U.S. patent No. 5,214,066 (May 25, 1993).

Balasubramaniam teaches PYY (column 2) and a pharmaceutical formulation comprising PYY (columns 14-16). The human PYY comprises amino acids 22-26 of SEQ ID NO: 2 of the present invention and the amino acid residues recited in claims 23-29 (column 2). Balasubramaniam teaches treating gastrointestinal disorders that are associated with excess intestinal electrolyte and water secretion as well as decreased absorption, such as infectious or inflammatory diarrhea, or diarrhea resulting from surgery (column 16) comprising administering PYY to a mammal, such as a human (column 6, lines 43-47). Inflammatory diarrhea includes Crohn's disease (column 7), a form of inflammatory bowel disease. The intestinal damage caused by these gastrointestinal disorders necessarily comprises a morphological damage, such as ulceration and those listed in claims 30 and 32. The histologic features of inflammatory bowel diseases such as ulcerative colitis or Crohn's disease comprise ulcer as evidenced by U.S. patent No. 5,214,066 (column 7, lines 1-7; column 1, lines 49-51).

Balasubramaniam also teaches that PYY inhibits gut motility and blood flow, attenuates basal and secretagogue-induced intestinal secretion in humans. Balasubramaniam further teaches that PYY plays a physiological role in regulating intestinal secretion and absorption, serving as natural inhibitors of diarrhea (column 1, lines 35-54; column 6,

lines 43-67). Balasubramaniam further teaches that the compounds can be administered orally or parenterally (intravenously or subcutaneously) (column 14). The daily dose in the case of oral administration is typically in the range of 0.1 to 100 mg/kg body weight, and the daily dose in the case of parenteral administration is typically in the range of 0.001 to 50 mg/kg body weight (column 16).

Accordingly, the teachings of Balasubramaniam meet the limitations of claims 1, 2, 5, 10-12, 22-30, and 32.

Response to Applicants' argument

Applicants argue that that U.S. patent No. 5,214,066 merely teaches an experimental animal research model in which ulcerations are induced which mimic ulcerations that may be observed in certain bowel disease states. Applicants argue that this does not mean demonstrate that all such bowel disease, or even all stages of, e.g., Crohn's disease necessarily comprise ulceration. Citing the reference of Louis et al., Applicants argue that the behavior of Crohn's disease may be classified according to severity and nature of symptoms and clinical aspects at various stages of the disease. Applicants argue that such classification may be employed to distinguish between "primarily penetrating, primarily fibrostenotic, or primarily inflammatory". Applicants argue that Crohn's disease, and indeed inflammatory bowel disease as a whole, do not comprise ulceration with absolute certainty.

Applicants' argument has been fully considered, but is not deemed to be persuasive for the following reasons. First, Louis et al do not teach, by any means, that Crohn's diseases do not comprise ulceration. Secondly, Crohn's disease is defined as "a chronic, sometimes fatal, inflammatory disease of the gastro-intestinal tract, esp. the ileum and colon, characterized by ulcers, fissuring, and fistulæ" (Oxford English Dictionary). Thirdly, U.S. patent No. 5,214,066 teaches that the histologic features of inflammatory bowel diseases such as ulcerative colitis or Crohn's disease comprise ulcer (column 7, lines 1-7; column 1, lines 49-51). Finally, WO 2004/035078 A1 (International filing date: October 15, 2003; Pub. date: April 29, 2004) also teaches "Crohn's disease is characterized by inflammation, thickening and ulceration of the bowel wall" (page 5, lines 14-21). Accordingly, Balasubramaniam inherently teaches a method of treating an intestinal damage comprising ulceration.

Claim Rejections Under 35 U.S.C.§103 (a)

(i). The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

(ii). Claim 14 is rejected under 35 U.S.C. 103(a) as being unpatentable over Balasubramaniam (U. S. Patent No. 5,604,203, Feb. 18, 1997) evidenced by U.S. patent No. 5,214,066 (May 25, 1993), as applied to claims 1, 2, 5, 10-12, and 22-32

above, and further in view of Dumont et al. (Brain Res. Mol. Brain Res. 26: 320-324, 1994).

Balasubramaniam teaches a method of treating an intestinal damage comprising an ulceration comprising administering a pharmaceutically active formulation of PYY to a human subject evidenced by U.S. patent No. 5,214,066 (May 25, 1993), as applied to claims 1, 2, 5, 10-12, and 22-32 above.

Balasubramaniam fails to teach the method of claim 14, comprising administering PYY[3-36].

Dumont et al. teach a PYY agonist, PYY[3-36] that binds PYY receptors (see Abstract).

Therefore, it would have been obvious to one having ordinary skill in the art at the time the invention was made to use PYY[3-36] in the method of treating a gastrointestinal disorder, such as Crohn's disease (a form of inflammatory bowel) as taught by Balasubramaniam with a reasonable expectation of success. One would have been motivated to do so because Balasubramaniam teaches PYY and PYY functional analogs can be used to treat a gastrointestinal disorder, such as Crohn's disease (first paragraph of column 7), whereas PYY [3-36] that binds to PYY receptors is expected to have the similar effect in treating a gastrointestinal disorder, such as Crohn's disease.

Response to Applicants' argument

Applicants argue that Balasubramaniam fail to teach a method of treating intestinal damage comprising administering a pharmaceutically active of PYY or a PYY agonist polypeptide as instantly claimed. Applicants argue that Dumont fails to cure the deficiencies of the teachings of Balasubramaniam. Applicants argue that Dumont fails to teach or suggest that ulceration is necessarily a morphological damage that accompanies any intestinal bowel disorder. Applicants' argument has been fully considered, but is not deemed to be persuasive for the reasons set forth above.

(iii). Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Balasubramaniam (U. S. Patent No. 5,604,203, Feb. 18, 1997) evidenced by U.S. patent No. 5,214,066 (May 25, 1993), as applied to claims 1, 2, 5, 10-12, and 22-32 above, and further in view of Murch et al. (U. S. Patent No. 6,046,179, Apr. 4, 2000).

Balasubramaniam teaches a method of treating an intestinal damage comprising an ulceration comprising administering a pharmaceutically active formulation of PYY to a human subject evidenced by U.S. patent No. 5,214,066 (May 25, 1993), as applied to claims 1, 2, 5, 10-12, and 22-32 above.

Balasubramaniam does not explicitly teach the intestinal damage associated with ulcerative colities.

However, it would have been obvious to one having ordinary skill in the art at the time the invention was made to apply method of Balasubramaniam to treat ulcerative colities (a form of inflammatory bowel) with a reasonable expectation of success. One would have been motivated to do so because Balasubramaniam teaches that PYY can be used to treat inflammatory diarrhea, which includes Crohn's disease and irritable bowel syndrome (first paragraph of column 7), whereas symptoms of ulcerative colities and Crohn's disease are similar and are often hard to differentiate as taught by Murch et al. (column 7, last paragraph to top of column 8).

Conclusion

No claims are allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruixiang Li whose telephone number is (571) 272-0875. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on (571) 272-0835. The fax number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published

applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, please contact the Electronic Business Center (EBC) at the toll-free phone number 866-217-9197.

/Ruixiang Li/
Primary Examiner, Art Unit 1646

Ruixiang Li, Ph.D.
December 27, 2009